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| 22850 7590 05/27/2009 OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314 | | | | |
| EXAMINER WINTERBERG, NISSA M | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/539,614

Applicant(s)

PETERET ET AL.

Examiner

Nissa M. Westerberg

Art Unit

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 - 21, 23 - 27 is/are pending in the application.
- 4a) Of the above claim(s) 6, 9 - 14, 21, 23 - 26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 - 5, 7, 8, 15 - 20, 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-85/08)
Paper No(s)/Mail Date See Continuation Sheet
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :8/12/05, 2/19/08, 5/16/08, 4/14/09.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I and the species as in claim 5 in the reply filed on April 2, 2009 is acknowledged. The traversal is on the grounds that the claims of groups I and II are integrally linked as method of making a product and the use thereof. When taken as a whole, there is technical relationship between the groups when the groups are taken as a whole. Unity of invention is present if the claims are drawn to a product, process specially adapted for the manufacture of said product and the use of said product." A search of all the claims would not impose a serious burden on the office.

These arguments are not persuasive because the groups must have the same special technical feature among the inventions of the various groups. Groups in which there is a common technical feature between the various groups is a special technical feature when it makes a contribution over the cited prior art. As described on p 2 - 3 of the Restriction Requirement mailed March 2, 2009, there is not a common technical feature between the groups identified by the Examiner so therefore the groups do not share a common technical feature so they cannot have the same special technical feature and do not possess unity of invention. See 37 CFR 1.475(a) and 37 CFR 1.475(e). Serious search burden is not a requirement for restriction of national stage applications.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

2. Claim 1 is objected to because of the following informalities: lines 3 – 5 contain a grammatical error. "Substrates for *applications as food* supplements for humans or animals" would make more sense when a word like "such" is inserted so the phrase states "applications such as food supplements". Appropriate correction is required. Please note that correction to include the phrase "such as" may raise an issue of indefiniteness under 35 USC 112, second paragraph.
3. Claims 27 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 already requires the present of one or more spray devices (line 9), the same limitation recited in claim 27.

Claim Rejections - 35 USC § 112 1st Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. None of the cellulose derivatives other than hydroxypropyl methyl cellulose meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus of cellulose derivatives encompassed by the claim, since there is no description of the structural relationship of these derivatives provided in the specification and Applicant has not provided a description as to how the base molecule may be changed while remaining a derivative.

Claim 3 is also rejected under 35 U.S.C. 112, first paragraph because no information as to where it would appropriate for the addition of further pharmaceutical excipients would or would not be appropriate is provided.

Claim Rejections - 35 USC § 112 2nd Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1 – 5, 7, 8, 15 – 20 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the limitation "said purposes" in line 5. There is insufficient antecedent basis for this limitation in the claim.

8. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. "Film-forming agent" is generally thought of as a particulate compound or polymer, as exemplified by Applicant in the claim. However, the film-forming agent may optionally comprise further pharmaceutical excipients. Additional ingredient would seem to render it a film-forming coating *composition*, rather than a film-forming coating *agent*. Please clarify.

9. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what is meant by the phrase "spray device as fixed installation." No information or definition of the devices and/or configurations that would meet this limitation are provided in the specification. Please clarify.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Bogentoft et al. (US 4,289,795).

Bogentoft et al. disclose pharmaceutical granules with a gradient coating (see figures) in which the active component, which reads on a further substance, decreases (abstract), resulting in a concentration gradient from the inside to the outside relative to the dried film coating.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) **MPEP 2113**. Whether the ingredients whose concentrations varies over time are mixed in a container prior to spraying, as in Bogentoft et al., or are sprayed from two separate containers and the ingredients mixed after spraying, as in the instant claims, the product

produced by these two methods has the same product and Bogentoft et al. anticipates the instant claim even though they are produced by different processes.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1 – 4, 18 – 20 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bogentoft et al. (US 4,289,795) and Abletshauser et al. (J Controlled Release, 1993, cited on August 12, 2005 PTO-1449).

Bogentoft et al. discloses a method of preparing a particle or coated granule wherein the concentration of active substance decreases towards the surface in a continuous coating operation (abstract). The non-active substance can control the release rate of the polymer and can be a variety of polymers, including polyacrylates, polymethacrylates or cellulose derivatives (col 3, ln 24 – 42). The particle employed as a core may consist of active agent alone or mixed with other active or inactive ingredients and are preferably spherical granules (col 3, ln 54 – 63). The process is carried out in a fluid-bed apparatus or coating pan (col 3, ln 43 – 48), apparatuses which read on fixed installations. The solutions of the substances whose concentration are varied are mixed prior to the solutions being sprayed onto the granules (col 4, ln 19 – 30).

Bogentoft et al. does not disclose a process in which the two components are in separate containers, are then sprayed from at least two separate nozzles so that the spray beams overlap, allowing for mixing of the ingredients during the spraying process.

Abletshauser et al. discloses the simultaneous fluidized bed spraying process in which the two liquid solutions are sprayed from a spray device and allowed to mix (p

150, col 2 ¶ 3) rather than being mixed and then sprayed. This simultaneous spraying can be achieved by means of two spray devices with a total of two nozzles mounted in the fluidized bed, allowing for more effective and faster drying process (p 152, col 2, ¶ 2 and figure 1).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to spray the ingredients using two nozzles as taught by Abletshuaser et al. to achieve the gradient coated pharmaceutical preparation as taught by Bogentoft et al. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because Abletshuaser et al. discloses that simultaneous spraying of two different solutions, rather than mixing the two solutions prior to spraying, can be used to coat pharmaceutical formulations. Changes in the sequence of adding ingredients are *prima facie* obvious (see MPEP 2144.04). By altering the flow rates of the two separate ingredients over time, the gradient formulation taught by Bogentoft et al. to allow for constant release of the active agent can be achieved.

16. Claims 1 – 5, 7, 8, 15, 16, 18 - 20 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bogentoft et al. and Abletshuaser et al. as applied to claims 1 – 4, 18 – 20 and 27 above, and further in view of Odidi et al. (US 6,479,075).

As discussed above, Bogentoft et al. and Abletshuaser et al. discloses a method of preparing a pharmaceutical product with a gradient coating wherein the ingredients are allowed to mix after being sprayed from multiple nozzles in an apparatus such as a

fluidized-bed. Abletshauser et al. also compares the simultaneous application of a layer with the sequential application of multiple layers and found that simultaneous application was more effective and dried faster (p 152, col 1, ¶ 2).

Neither reference discloses a substrate comprised of an acid-sensitive active ingredient, such as proton pump blocker like omeprazole, that is coated with a gradient of wholly or partly neutralized (meth)acrylate copolymer and a less neutralized (meth)acrylate copolymer wherein the concentration of the less neutralized copolymer increases from the inside to the outside.

Odidi et al. discloses enteric coated dosage form of acid labile compounds such as omeprazole or lansoprazole (col 2, ln 23 – 31) which contains a protector coat layer between the acid labile substance and the enteric coating (col 2, ln 41 – 49). The protector layer enhances the storage stability by acting as an acid sequestering compound and is most preferably made from EUDRAGIT® E, a dimethylaminoethyl methacrylate and neutral methacrylate copolymer (col 3, ln 14 – 19, ln 54 – 60), which reads on a (meth)acrylate copolymer comprising anionic groups which are wholly or partly neutralized. The protector coat can contain other excipients such as plasticizers (col 3, ln 64 – 66). The enteric coating applied can be composed of a variety of ingredients, including type A, B or C methacrylic acid polymer types or mixtures thereof (col 4, ln 18 – 37). Such methacrylic acid polymers are (meth)acrylate copolymers that comprise anionic groups that are less neutralized than the polymers of the protector layer.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use the method taught by Bogentoft et al. and Abletshauser et al. to prepare a pharmaceutical composition as disclosed by Odidi et al. An enteric coating is required to protect acid labile ingredients such as omeprazole from degradation in the stomach, but the acidic nature of enteric polymers such as the methacrylic acid polymers can also cause degradation of the active ingredient over time as the dosage form is stored. This can be prevented by the use of a protector coat that acts as acid sequestering layer, such as a layer in which acidic groups have been neutralized such as in EUDRAGIT® E. Abletshauser et al. discloses that the mixing of ingredients while being sprayed is a more efficient way to coat particles than sequential application of layers. By applying these two polymers simultaneously and in the gradient fashion as disclosed by Bogentoft et al., the final pharmaceutical product would have a high concentration of the protector layer in contact with the acid-labile, active ingredient core that would decrease as the fraction of the enteric coating increased. The final dosage form would then essentially have an enteric outer coating and an inner protector layer that was applied in a single coating step rather than two separate layers applied in two separate coating steps.

The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each

ingredient and plasticizer to add in order to best achieve the desired results for the process steps and in the physical properties of the product that is produced.

17. Claims 1 – 4, 17 – 20 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bogentoft et al. and Abletshauser et al. as applied to claims 1 – 4, 18 – 20 and 27 above, and further in view of Walter (US 6,270,801).

As discussed above, Bogentoft et al. and Abletshauser et al. discloses a method of preparing a pharmaceutical product with a gradient coating wherein the ingredients are allowed to mix after being sprayed in an apparatus such as a fluidized-bed.

Neither reference discloses the use of a two-fluid nozzle.

Walter discloses that two-fluid nozzles (part **14**), each with a liquid supply, can be used to introduce solutions into a coating apparatus (figure 1 and col 6, ln 27 – 29).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use the two-fluid nozzle disclose by Walter in the gradient coating method disclosed by Bogentoft et al. and Abletshauser et al. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because Walter discloses the use of such equipment in the coating of granulate particulate materials for the food or pharmaceutical industries (col 5, ln 28 – 34).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Examiner, Art Unit 1618

NMW